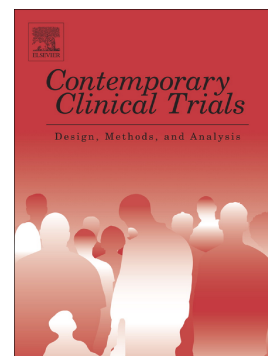


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Link-me: Protocol for a randomised controlled trial of a systematic approach to stepped mental health care in primary care

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Abstract

Primary care in Australia is undergoing significant reform, with a particular focus on cost-effective tailoring of mental health care to individual needs. Link-me is testing whether a patient-completed Decision Support Tool (DST), which predicts future severity of depression and anxiety symptoms and triages individuals into care accordingly, is clinically effective and cost-effective relative to usual care. The trial is set in general practices, with English-speaking patients invited to complete eligibility screening in their general practitioner's waiting room. Eligible and consenting patients will then complete the DST assessment and are randomised and stratified according to predicted symptom severity. Participants allocated to the intervention arm will receive feedback on DST responses, select treatment priorities, assess motivation to change, and receive a severity-matched treatment recommendation (information about and links to low intensity services for those with mild symptoms, or assistance from a specially trained health professional (care navigator) for those with severe symptoms). All patients allocated to the comparison arm will receive usual GP care plus attention control. Primary (psychological distress) and secondary (depression, anxiety, quality of life, days out of role) outcomes will be assessed at 6 and 12 months. Differences in outcome means between trial arms both across and within symptom severity group will be examined using intention-to-treat analyses. Within trial and modelled economic evaluations will be conducted to determine the value for money of credentials of Link-me. Findings will be reported to the Federal Government to inform how mental health services across Australia are funded and delivered in the future.

Keywords: Mental health, primary care, general practice, randomised controlled trial, stepped care, decision support tool, care navigation

Date and version number

06.08.2018 Version 1

Abbreviations

ATAPS	Access To Allied Health Psychological Services
CPT	Clinical Prediction Tool
DST	Decision Support Tool
EAG	Evaluation Advisory Group
EQ-5D-5L	Euroqol 5-dimension quality of life questionnaire (5-level version)
GAD-2 / GAD-7	Generalised Anxiety Disorder scale (2-item / 7-item version)
GP	General Practitioner
HREC	Human Research Ethics Committee
ITT	Intent to treat
K10 / K10+	Kessler Psychological Distress Scale (10-item / 14-item version)
MBS	Medicare Benefit Schedule
MI	Motivational interviewing
NPT	Normalisation Process Theory
PBS	Pharmaceutical Benefit Scheme
PHN	Primary Health Network
PHQ-2 / PHQ-9	Patient Health Questionnaire (2-item / 9-item version)
PMHC MDS	Primary Mental Health Care Minimum Data Set
QALY	Quality Adjusted Life Year
RUQ	Resource Use Questionnaire
SC	Steering committee

Background and rationale

Psychiatric disorders are a leading cause of disability worldwide, and despite significant investment in their identification and treatment, the global burden of disease associated with these disorders continues to rise [1]. Although effective treatments exist, there is increasing recognition that some people who may benefit from these miss out, and others may receive treatments that are more intensive than required for their level of illness [2-4]. Addressing this imbalance has been the focus of trials of models of collaborative care and stepped care in both the UK and the US. To date, however, these have delivered only small to moderate gains in health outcomes in the short- to medium-term [5, 6]. At the same time, there is increasing recognition of the burden that multimorbidity places upon the individual and the health care system, but there is limited evidence for interventions that improve outcomes for affected individuals treated in primary care [7, 8].

In Australia, efforts to reduce the burden of psychiatric disorders have centred around providing access to psychological services through general practitioner (GP) referral, with substantial investment in the *Access To Allied Health Psychological Services* (ATAPS; 2001 – 2016) and the *Better Access to Psychiatrists, Psychologists and General Practitioners through the MBS* initiatives [9]. Uptake of psychological services under these initiatives has been considerable; in 2016-17 alone, more than one million Australians received psychological treatment under the Better Access scheme [10]. Under these initiatives, treatment is limited to a maximum number of sessions per individual per year (10-18 depending upon the scheme) and there is the potential for both under- and over-treatment [3].

It has been suggested that Australia could benefit from a more targeted approach to matching the intensity of service provision to individual need [11]. To this end, in 2015 the Australian Government introduced major service delivery reforms, including an expanded role for Primary Health Networks (PHNs; see Box 1) in the planning and commissioning of primary mental health care services [12]. Specifically, PHNs were tasked with facilitating the introduction of stepped care, defined as a continuum of primary mental health services within a person-centred approach, where a range of service types are available within local regions to better match both individual and population need [13].

In this context, three PHNs have been selected to work with the University of Melbourne on Link-me, a randomised controlled trial (RCT) of a systematic approach to stepped mental health care. Link-me builds on over 15 years of research, including the development of a clinical prediction tool (CPT) from a ten year longitudinal cohort study of depression and preliminary testing of that tool in a systematic approach to identification of and tailored treatment for depression in the Target-D RCT [14-16]. Link-me uses a Decision Support Tool (DST) completed by patients in the general practice setting to predict the future severity of depressive and anxiety symptoms, and triage patients into high or low intensity care accordingly.

Aim

Link-me aims to determine whether systematic identification of patients' symptom severity using a DST in general practice and provision of tailored treatment recommendations is clinically and cost effective compared to usual care.

Method

Trial design

Link-me is a stratified individually randomised controlled trial, with general practice patients randomly allocated to receive either the trial intervention or usual care with a 1:1 ratio. Patients are stratified by general practice and by predicted depressive and anxiety symptom severity at three months, as determined by the DST.

The DST builds on a CPT developed for the Target-D RCT which predicts the severity of depressive symptoms at three months [15, 16]. The Link-me DST has been adapted with advice from an Expert Advisory Panel to include the prediction of anxiety symptoms as well as depression, thereby capturing the majority of mental health presentations in the Australian population [17]. It comprises

23 items¹ assessing current depressive symptoms, current anxiety symptoms, lifetime history of depression, gender, living situation, ability to manage on available income, self-rated general health, and presence of chronic illness that affects the ability to carry out daily activities. Two prognostic models embedded within the DST use participant responses to these items to predict symptom scores for anxiety and depression at three months. Based on their predicted score, participants are classified into one of three symptom severity groups (minimal/mild, moderate, and severe) and receive information relevant to their group and trial arm allocation (see 'Intervention' below). More information about the DST is provided in Supplementary file 1.

This trial protocol has been developed using the SPIRIT guidelines for intervention trial designs [18].

Trial setting

Link-me is set in general practices located within the three participating PHN catchment areas, across three states in Australia (Victoria, New South Wales and Queensland). Demographic and geographical characteristics of the PHNs vary; two are located in large cities and extend to outer urban boundaries; the third covers a large regional area. General practice sizes differ and the mix of staff and availability of allied health services is likely to be variable. We anticipate at least 18 practices will participate from across the three PHNs, in order to recruit sufficient participants (see 'sample size' below).

General practices will be invited to take part in the study by a regional trial coordinator employed by the relevant PHN. Eligibility criteria for general practices include: 1) seeing at least 100 adults aged 18-75 per day; 2) using patient medical records software (to enable patient records to be easily updated with information relevant to Link-me participation); 3) agreement for a trained health professional to work in the practice to provide support for patients triaged into the severe symptom group; and 4) agreement to follow the trial protocol. In the event of insufficient eligible practices being identified, criteria 1 and 2 may be relaxed to allow additional interested practices to participate. A representative from each practice will be asked to complete a brief survey at the time of recruitment to allow a description of the study sites.

Participants

Participants in the trial will be adults recruited in the waiting room of each participating general practice. Eligibility for the trial will be established in a two-stage process. First, practice (e.g. receptionists) or trial staff (e.g. research assistants) will approach all adult patients in the waiting room (regardless of reason for presentation) and through a brief discussion, establish whether the patient is:

- Aged 18–75 years;
- Sufficiently proficient in English to participate;
- Able to provide a phone number and email address; and
- A Medicare card holder (i.e., a permanent resident of Australia and therefore eligible for federally funded healthcare);
- Able to provide informed consent.

¹ The previous CPT on which the DST was based comprised 17 items and predicted depression only. The additional 6 items relate to current anxiety symptoms and are included in the prognostic model for anxiety at three months.

Patients who demonstrate signs of acute health problems (e.g. vomiting or in obvious pain) will not be excluded from the study, however, recruiters will be encouraged to consider approaching them at another time (e.g., on their next visit to the practice).

All patients who indicate to the recruiter that they meet the above criteria will be invited to take part in the second step of the eligibility screening process. This will entail completing a brief survey on a hand-held tablet device. The survey will comprise a series of demographic questions as well as a brief assessment of current mental health need. Patients will be eligible for Link-me if they report at least one of the following:

- a score of 2 or more on the 2-item version of the Patient Health Questionnaire [PHQ-2: 19];
- a score of 2 or more on the 2-item version of the Generalised Anxiety Disorder scale [GAD-2: 20];
- current use of medication for mental health problems.

Patients who do not meet these criteria will be exited from the survey at the point at which they are no longer eligible for the trial, and will see a screen thanking them for their time and requesting that they return the tablet device to reception. Recruiters will be trained to check in with patients who agree to complete the survey and offer assistance or answer questions where required.

Consent

Following this two stage screening process, eligible patients will receive an invitation to take part in Link-me. On the tablet device, they will read a plain language statement about the trial and will be asked to give consent to participate. The plain language statement will also advise participants that they will be asked for separate consent to access routinely collected administrative data about their use of health services and prescription medicines (for details of this data, see 'Economic evaluation' below). In Australia, individual consent is required to access this information. Consenting to provide access to this data is optional and will not affect an individual's participation in the trial itself nor the services that they receive. Until consenting to the trial, all data entered into the tablet is anonymous; individuals will only be asked to provide their name and contact details if they agree to take part.

Immediately after providing consent, all participants will complete baseline measures and the DST assessment on the tablet device. Stratification into symptom severity groups and randomisation will occur at the point of assessment completion. After viewing the information relevant to their symptom severity group and trial arm on the tablet device, all participants will be automatically sent an email including: a) the trial plain language statement; b) a list of community-based services and support lines²; and c) further details about the request to access routinely collected health service use data and a link to provide online consent for the Australian Government to release this data to the researchers.

Intervention

Intervention arm

Participants randomly allocated to the intervention arm will receive [14]:

² For example, Lifeline (<https://www.lifeline.org.au>) which provides support to people experiencing a crisis.

- Feedback on their DST responses (a summary of the areas in which they appear to be functioning well, and where their answers indicate they may be experiencing difficulties);
- An opportunity to set mental health priorities (selecting up to two of the areas identified as being difficult) and reflect on current motivation to address these priorities;
- A treatment recommendation matched to predicted symptom group (minimal/mild or severe), described in more detail below.

GPs will be notified of those patients who are allocated to the intervention arm and their treatment recommendation. Notifications will be provided in writing by the care navigator (Box 2), a professional engaged specifically in the trial to communicate this information to GPs and deliver the intervention for participants in the severe symptom group. The care navigator will use a standardised template pre-populated with the patient's details, accessed through an online administration portal. This will occur following the consultation so as not to distract from the reason for the patient's visit, which may not be related to their mental health. The GP will be encouraged to discuss the participant's treatment recommendation at his or her next consultation (although it is up to the GP whether or not he or she does so). This process, in combination with the person-centred approach to recommending treatment as part of the DST, is designed to improve workflow and treatment engagement. It builds on evidence showing that simply alerting the GP to a patient's score on completion of a screening tool does not improve health outcomes [21, 22], and our experience in the Target-D trial [15].

Treatment recommendations for the minimal/mild symptom group

Participants predicted to have minimal/mild symptoms of depression and anxiety in three months' time and randomised to the intervention arm will be provided with low intensity service options across four modalities, including online, telephone, mobile app, or in person services (see example in Figure 1). The service options will be matched to the areas of difficulty identified in the DST and/or prioritised by the participant. After a review of the published evidence, service options were selected based on evidence of the effectiveness of the service itself (e.g. MindSpot [23]), the principles underpinning it (e.g. a cognitive behavioural therapy-based app), or the behaviours it facilitates (e.g. a local walking group was considered to encourage exercise) [24].



Figure 1. Example screenshot of low intensity service options for a patient who identified mood as a priority area [23, 25, 26].

As well as viewing their treatment recommendations on the Link-me tablet in the practice waiting room, participants in the minimal/mild symptom group will also receive a copy of the recommendation with links to the relevant services via email (attached along with the plain language statement to the email described above). No additional measures will be taken to encourage treatment adherence. Participants will be free to follow the recommendation or not, and free to discuss it with their GP or not.

Box 1. DEFINITIONS

Primary health networks: Government-funded commissioning bodies established to increase the efficiency and effectiveness of medical services for patients (including but not limited to mental health services), particularly those at risk of poor health outcomes, and improve coordination of care to ensure patients receive the right care in the right place at the right time [27].

Low intensity services: Mental health interventions that minimise or eliminate specialist therapist contact time. Low intensity services are typically low cost and can be accessed without referral; focus on early intervention, self-help, and skill development; may be delivered to individuals or groups; and may be delivered in person, over the telephone or online [28].

Treatment recommendations for the severe symptom group

Participants identified as being likely to experience severe symptoms of depression or anxiety in three months and randomised to the intervention arm will be offered a model of clinical care coordination comprising care navigation, care planning and care packages aimed at accessing services likely to improve mental health (Box 2). This intervention is informed by the principles of collaborative care [5, 29-32] and informed by recognition that people in this group are often experiencing mental-physical multimorbidity and have multiple interacting physical, mental and social needs [33]. Our intervention has been designed to improve access to appropriate mental health treatment and to lifestyle interventions that might assist overall health. The care navigator role is described in full in Box 2 and involves:

- Up to eight structured appointments with the care navigator to develop and implement a structured care plan to address the priorities set by the patient in the DST. Appointments can be conducted face to face in the practice or over the phone, depending on patient preference. For the majority of these eight appointments, the focus will likely be on the implementation of the plan, including providing support to identify and access appropriate services;
- An explicit patient-centred focus, with the plan development and implementation led by the patient's own priorities and goals. These may be articulated spontaneously or with assistance from the care navigator;
- Access to additional funding via a 'care package' as described in Box 2;
- Close collaboration between the care navigator and GP, with the care navigator acting as clinical companion to the GP and GP retaining final responsibility for endorsement of the care plan;
- Explicit short-term involvement of the care navigator, with a clear plan for the GP and patient to continue working towards the patient's goals after the end of the care navigator's involvement in the patient's care. This will generally occur after approximately three months, but the exact duration of care navigation is flexible and can be adapted to patient need.

To encourage treatment adherence, patients in this group will receive reminders of upcoming appointments with their care navigator via phone, email, or SMS. Non-attenders will be similarly contacted to reschedule missed appointments. Care navigators will seek advice and assistance from GPs in encouraging patient adherence, for example discussing strategies to reach a patient who the care navigator has been unable to reach by phone to schedule an appointment.

BOX 2: THE CARE NAVIGATOR ROLE & CARE PACKAGE OPTIONS

Link-me care navigation is defined as a model of clinical care coordination delivered in general practice, in which a trained health professional (care navigator) works collaboratively with patients and GPs to develop and implement a structured mental health care plan that meets patient needs. The care navigator provides short-term assistance to identify and link patients in with appropriate services.

The care navigator role has been designed to be performed by a registered health professional and does not require specialist mental health training. To help patients identify what they want to

achieve, and how, care navigators will receive training in the principles of motivational interviewing (MI) [34] from an internationally recognised MI trainer and qualified psychologist. Initial training comprises a one-day face-to-face workshop on MI skills, with refresher sessions once per month (1 hour by phone) and up to 4 times per year (up to half day face-to-face). Care navigators will also be provided with written MI resources to refer to as needed.

Care navigators will have access to a secure online administration portal to support their work with the patients in the severe symptom group. The portal will auto-populate with patients completing the DST in real time, providing care navigators with contact details and DST results for patients allocated to the care navigation intervention. In appointments with patients, care navigators will be able to use the portal to step through the process of developing a structured plan, with prompts to enquire about and record the patient's current situation and past history (including medical, social, and psychological factors), consider treatment preferences, check current symptoms and review DST responses, set treatment goals and identify actions to take, and review progress. At each appointment, care navigators will add to or change the plan as needed. Each update saves as a separate file so care navigators can review previous versions at any time. The online administration portal also provides access to a structured suicide risk assessment which can be used as needed. After each appointment care navigators will complete an appointment summary in the portal, recording details such as duration and modality as well as their reflections on what went well and the challenges they faced in the appointment.

Importantly, the care navigator role is not one that provides mental health treatment. Rather, the key role of the care navigator is to act as a clinical companion to the GP and to support the patient to identify and access services required to improve mental health. For many patients, these services might include those available through existing programs and funding sources (e.g., mental health professionals, drug and alcohol services, pharmacists, allied health). For others, a 'care package' may be required to improve access to care.

Care packages

Care navigators in the Link-me trial will have access to care package funding to assist in helping patients access additional services that may not be currently accessible (e.g., because they are not commissioned by PHNs or are not Government subsidised [i.e. out of pocket cost is too high]) but are identified as necessary to improve the patient's mental health outcomes. PHNs will be the fund-holders and administrators for the care package funding, which has been allocated at an amount of AU\$2000 per expected participant, although it can be used flexibly across the pool of participants receiving care navigation. Care navigators will make requests to the PHN to access care package funding for a participant according to a guidance document outlining how and when this funding may be used. Services purchased with this enhanced care package funding will typically be health services delivered by a clinical health professional, but may be services delivered by others as ancillary to formal health care. Funding may support, for example, additional or alternative psychological services, access to other health professionals such as exercise physiologists or dietitians, peer support services, vocational or educational support services, yoga or mindfulness courses, family support services, and other individual assistance provided through community support agencies. Services accessed through care packages may be either evidence-based, or encourage behaviours or activities which have been shown effective in managing mental health [24]. Out of scope are goods, inpatient care, and services funded through existing programs. Use of care

package funding will require GP agreement that the nominated service may improve the patient's mental health. In addition, services that are not explicitly listed as in or out of scope in the written guidance provided to care navigators will be discussed with the National Trial Coordinator and/or Department of Health project team prior to implementation.

Comparison arm

Participants predicted to have minimal/mild or severe symptoms at three months and randomly allocated to the comparison arm will continue to receive usual care from their GP. After completing the DST assessment, participants in this arm will receive some attention control in the form of a prompt on the tablet device to speak with their GP regarding any concerns they have, and the email described above containing a list of contacts for community-based resources and services.

Moderate symptom group

Participants whose scores fall between the cut-offs for minimal/mild and severe groups (i.e., those with moderate symptoms) will not be randomised as they are considered to be appropriately served by the existing mental health service options available via their GP. After participants in this group complete the DST assessment they will be prompted to discuss any concerns about their mental health with their GP and provided with a list of contacts for community-based resources and services via email as described above. While not a focus of this trial, they will be asked to complete outcome assessments at follow-up as per randomised participants, to inform further validation of the DST algorithm.

Modifications and concomitant care

The trial interventions are flexible by design and no substantive modifications are anticipated. Patients in both the minimal/mild and severe intervention groups will be free to take up their treatment recommendation or not, and may discontinue treatment at any time. For patients allocated to the care navigation intervention, care navigators will document reasons for discontinuation where known, in order to inform the embedded process evaluation.

All participants, regardless of trial arm allocation and predicted symptom severity group will be free to continue any treatment they were receiving at entry to the trial, including both pharmacological and psychological interventions. Data collection procedures will include assessment of concomitant care before, during, and after the intervention phase of the trial. Additionally, for patients in the severe symptom intervention group, concomitant care will be identified and recorded by care navigators as part of the care navigation process.

Allocation and blinding

Randomisation will be triggered automatically within the trial's online administration portal, after the participant has provided consent and completed the DST assessment, ensuring allocation concealment and minimising reporting and selection bias. The allocation sequence will be computer generated consecutively, using a biased coin algorithm [35].

Individuals will be randomised instead of general practices for two key reasons. First, the intervention will be delivered at the individual level rather than the practice level. Second, the risk of contamination (i.e., participants in the comparison arm receiving a dose of the intervention) will be low because a) no one involved in patient recruitment or intervention delivery will have access to

the allocation schedule; and b) both GPs and care navigators will only be informed of participants allocated to the intervention arm:

- Severe symptom group: GPs will be unable to refer patients to the care navigator. They will not receive training in care navigation or have access to care packages, and will therefore be unable to deliver this model of care themselves,. Our experience using this approach in Target-D found that GPs are only aware of the patients receiving contact from the care navigator, are unable to estimate how many of their patients may be involved in the trial, and indicate that they have not altered their approach to care for patients not receiving care navigation;
- Minimal/mild symptom group: Participants will be recommended to access services based outside the practice, reducing the potential for practice-based contamination. We note however that the services recommended to this group are publicly available and may also be accessed by participants in the comparison arm as part of usual care. In follow-up assessments we will assess the number of participants in both arms who access these services.

Participants cannot be blinded to their treatment allocation due to the design of the intervention. Staff involved in participant recruitment may be unblinded if, upon completing the DST, participants mention to the recruiter the information displayed on the tablet. However as above, recruitment staff will not be able to use this information to influence future allocations. Finally, all trial analyses will be conducted by statisticians blinded to participants' allocation. However in order to support the process evaluation, relevant members of the research team will be partially unblinded and have access to care navigation information entered into the online portal.

Outcomes

Outcomes are assessed at trial enrolment and at 6 and 12 months after DST completion (Table 1).

Table 1. Schedule of participant completed assessments

	Enrolment	6 months	12 months
Demographics	•		
Psychological distress and days out of role (K10+)	•	•	•
Depression (PHQ-9)	•	•	•
Anxiety (GAD-7)	•	•	•
Quality of life (EQ-5D-5L)	•	•	•
Health service use (RUQ)	^a	•	•

^aIn order to minimise participant burden, the RUQ is not administered at baseline. Instead, health service use at this timepoint is assessed using a general item on the K10+ and routinely collected government data about health service use (e.g. appointments and referrals) for those who consent, assuming that most highly used services are captured in these datasets.

Primary outcome

The primary outcome is the difference in mean psychological distress scores between the intervention and comparison arms at arms at 6 months. Psychological distress will be assessed using

the 14 item version of the Kessler Psychological Distress Scale [K10+: 36]. The K10+ is an extension of the standard 10 item scale (the K10) which asks respondents to indicate how often in the past 4 weeks they have experienced certain symptoms (e.g., nervousness, hopelessness, fatigue, agitation, and depressed mood), using a 5-point Likert scale (where 1 = 'not at all' and 5 = 'all the time'). The additional four questions ask respondents to nominate the number of days totally and partially unable to study or work due to symptoms reported in the previous 10 questions, number of health professional consultations sought as a result of these symptoms, and the extent to which physical health problems were the main cause of distress.

Total scores are calculated as the sum of the standard 10 items and range from 10 to 50 (the additional four questions reported separately and do not contribute to the total score), with scores of 10-15, 16-21, 22-29, and 30-50 indicating low, moderate, high, and very high distress respectively [37]. The K10 has excellent internal consistency, and sensitivity and specificity in predicting formal psychiatric diagnosis [36]. Psychological distress was selected as the primary outcome as we considered a generic outcome measure more appropriate to the target population than one tied to a particular diagnosis, given that eligibility for the trial is not diagnosis-dependent. Further, the K10+ is the most widely used outcome measure in Australian primary mental health care, and in 2016 its use was mandated in all episodes of care delivered through PHN-commissioned services [38].

Secondary outcomes

Secondary outcomes include depressive symptom severity, anxiety symptom severity, and quality of life, and days out of role at 6 and 12 months, and the K10 at 12 months.

Depressive symptom severity will be assessed using the 9-item version of the Patient Health Questionnaire [PHQ-9: 39] which assesses the presence of the nine DSM symptoms of depression over the last two weeks using a 4-point Likert scale (where 0 = 'not at all' and 3 = 'nearly every day'). Total scores range from 0 to 27, with cut points of 5, 10, and 15 indicating mild, moderate, and severe depression, respectively [39]. The PHQ-9 is a validated diagnostic measure in primary care [40], with demonstrated efficacy and sensitivity as an outcome measure for treatment trials with a recommended Reliable Change Index [41].

Anxiety symptom severity will be assessed using the 7-item Generalised Anxiety Disorder scale [GAD-7: 42] which assesses the presence of generalised anxiety symptoms over the past 2 weeks using the same 4-point Likert scale as the PHQ-9. Total scores range from 0 to 21, with cut points of 5, 10, and 15 corresponding to mild, moderate, and severe anxiety symptoms. Internal consistency and test-retest reliability for the GAD-7 are both excellent. It has high construct, convergent, and discriminant validity, and correlates well with measures of depression and functioning, and with other measures of anxiety [42].

Days out of role will be measured using two of the additional four questions included in the K10+, which ask respondents to nominate the number of days they were totally or partially unable to study or work.

Quality of life will be assessed using the EQ-5D-5L, a self-report scale assessing health states across five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) [43]. Respondents rate the extent to which they have problems in each dimension on a 5-point scale, and indicate their overall health on a scale from 0 to 100. The EQ-5D-5L shows better discriminatory

power and convergent validity than the extensively validated EQ-5D-3L, on which the five dimensions are rated on a 3-point scale [44].

Economic evaluation

A comprehensive economic evaluation will be conducted, drawing on the EQ-5D-5L and information on health service use collected through:

- A self-report resource use questionnaire (RUQ), adapted from one used previously in Australian trials of mental health interventions [15, 45, 46]. The RUQ assesses the nature, frequency and duration of use of relevant health services (including low intensity services such as online programs and mobile phone apps) during the past 6 months, as well as the impact of mental health problems on productivity. The RUQ includes both forced choice, multiple choice, and free text options (text and number fields); see examples in Table 2. It comprises 68 items in total, although the number of questions presented to each individual varies depending on their responses; the minimum number of items a participant may be asked to complete is 19. Using Table 2 as an example, a participant indicating they have not seen a psychologist in the past six months will not see the two follow up questions about where they saw the psychologist and how much they paid.
- Where possible, information about health service use accessed from one or more of the following:
 - Medicare Benefits Schedule/Pharmaceutical Benefits Scheme (MBS/PBS): provides information on visits to health care providers, diagnostic tests, and prescription medications via Australia's universal health care system.
 - Primary Mental Health Care Minimum Data Set (PMHC MDS): captures data on each episode of primary mental health care including the type, modality and duration of the service, which type of health professional it was delivered by, and consumer co-payment (if any). PMHC MDS data will only be available for the subset of participants who have received a mental health service commissioned by their PHN, and have consented to being included in the PMHC MDS.
 - headspace, the National Youth Mental Health Foundation: captures data on youth mental health services provided through headspace centres nationally. headspace data will only be available for the subset of participants who are aged 18 – 25 and have used headspace services.

Table 2. Sample RUQ items

Item type	Item	Response options
Forced choice	In the past six months, have you seen a psychologist because of your mental health?	No Yes
Multiple choice	Where did you see the psychologist?	Doctor's room or other private practice General community health clinic Specialist community mental health clinic Community-based rehabilitation clinic

		Hospital outpatient clinic
		At a drug or alcohol service
		At your home
Number	On average, how much of your own money did you pay each time you saw a psychologist?	\$_____
Free text	In the past six months, what online therapy programs have you used for your mental health?	_____

Data collection and management

Surveys of practice and GP characteristics will be completed in hard copy at each participating practice and sent to the University of Melbourne via registered post or scanned and sent via email as a PDF. Each practice and GP will be assigned a unique ID, and survey responses and identifying information will be entered into a separate electronic database and stored securely on a password-protected University server. Any hard copy surveys provided to the University will be destroyed after the data have been checked, entered and cleaned.

A purpose-built online data collection system will be used to ensure efficient and secure collection of participant data via self-report questionnaires. At trial enrolment, this will involve completing the eligibility screening questionnaire, outcome measures, and DST on the tablet device in the general practice waiting room. In addition to the outcome measures described above, demographic questions will be embedded into the questionnaires completed during the enrolment process, including age, gender, education and employment, identification as Aboriginal and/or Torres Strait Islander, language spoken at home, and reason for GP consultation.

Data at each follow-up timepoint will be collected on the same online system used at enrolment. Two weeks prior to their due date for each assessment, participants will receive an automated email containing a link to the follow-up questionnaire, which they will be able to complete on any internet enabled device.

At each time point, participant responses to validated outcome measures will be coded according to published protocols for each measure, as described above. To minimise missing data, answers to all questions on each page will be required before the individual can move on. Data integrity will be enforced through the use of forced or multiple-choice items wherever possible. Valid value and range checks will also be built in for free text fields where appropriate. A data manager blind to participant allocation will check all outcome data to identify and, where possible, resolve errors prior to analyses being conducted by the statistician.

The online data collection system will automatically generate a unique number for each patient who commences the eligibility screening questionnaire, and all data related to that participant will be linked to this ID. Participants' trial information will not be released outside of the trial without their permission, except where maintaining confidentiality endangers the health or safety of the participant or someone else. Within the online system, identifying information will be visible in order

to allow GPs to be notified of their patients' treatment recommendation (for those allocated to the intervention group), delivery of the care navigation intervention (including use of care packages where relevant), completion of structured risk assessments where necessary, and participants to be contacted for reminders about survey completion at follow-up. At the end of the trial, the web developers will remove identifying information, leaving only the participant's unique number, then download all trial data. The de-identified database will then be stored securely and backed up regularly on a central password-protected University system.

Sample size

Our primary aim is to test for a difference in mean K10 scores between the intervention and comparison arms at 6 months. However, we also plan to conduct secondary analyses to test the differences in mean K10 scores between the trial arms for the minimal/mild symptom and severe groups, separately. As a larger sample size will be required for the sub-group analyses than for the primary analysis, we first determined the sample size required for the sub group analyses. We then determined that power of the study to test for the primary hypothesis based on the combined sample size required for the sub-group analyses.

Based on our *diamond* [47] and Target-D [15] studies we assume that around 15% of participants will fall into the moderate symptom group and be excluded from the trial analyses. Of the remainder, 76.5% will be identified as belonging to the minimal/mild symptom group and a smaller proportion (23.5%) will fall into the severe symptom group. Thus, the critical calculation is the sample size in the severe symptom group as we estimate a smaller proportion of participants to be stratified into this group by the DST.

Assuming 80% power and a 5% significance level for a two-tailed test for the sub-group analysis, we require 352 participants (176 per arm) in the severe symptom group to test for a standardised effect size of 0.3 (equivalent to a difference in means of 2.4 points on the K10). This effect size was selected based on previous trials of collaborative care interventions [5, 48]. For the minimal/mild symptom group, we anticipate a smaller effect size given that this group will have less room for improvement (i.e., lower K10 scores at baseline on average) and will receive less intensive treatment. Therefore, to detect a standardised effect size of 0.2 (equivalent to a difference in means of 1.6 points on the K10) we require 788 participants (394 per arm) in the minimal/mild symptom group. However, given the assumed unequal distribution of participants in the two symptom groups (76.5% vs 23.5%), it is likely the sample available for analysis will be 1,146 patients (573 per arm).

Based on these figures, the combined sample size of 1,498 (749 per arm) will provide over 90% power to detect a standardised effect size of 0.17 (equivalent to a difference in means of 1.3 points on the K10) for the primary outcome at 6 months. This minimal effect size is conservative, and assumes the worst-case scenario of no difference in K10 in the minimal/mild symptom group, but a detectable difference in mean K10 scores between the trial arms in the severe symptom group.

In order to allow for 50% attrition over 12 months, we aim to recruit a total sample of 2,996 patients at baseline. This baseline sample will comprise 704 participants (352 per trial arm) in the severe symptom group and 2,292 in the minimal/mild symptom group (1,146 per trial arm) (Figure 2).

Retention

To encourage retention at each follow-up assessment, participants will first be sent a primer postcard to remind them about the study and alert them to the fact that they will soon be asked to

complete their Link-me survey. Non-responders to the email survey will receive two email reminders, each a week apart, followed by up to four reminders via phone or text. Each reminder will also provide the option of completing the survey by telephone, in person at the participant's general practice, or via a hard copy sent and returned by post. Participants who still do not complete the survey will be offered the option of only completing the primary outcome measure (K10+).

At each follow-up assessment, participants who have not yet provided consent to release their health service use data will be provided another opportunity to do so, by either continuing to the consent form at the end of the online survey or clicking directly into the consent from an emailed link.

Patient recruitment

To achieve the required sample size, we anticipate that at least 78,000 patients will be invited to complete the eligibility screening survey in the waiting room (Figure 2). Based on our Target-D trial, we expect 60% of patients will complete the survey, 30% of whom will be eligible to participate in Link-me. Of these eligible patients, we project 25% of patients will consent to the trial and complete the DST. Data on the total number of patients attending each practice during the recruitment period will be sourced from practice software to enable the calculation of the proportion of the total patient population invited to participate.

Practice (e.g. receptionists) or trial staff (e.g. research assistants) will conduct a brief eligibility assessment and provide a short verbal description of Link-me as well as a brochure with further information including details of how to contact the trial team at the University of Melbourne should the patient have questions. Recruiters will then provide interested and eligible patients with the tablet device on which to complete the screening survey. All staff involved in patient recruitment will receive a 90 minute power point-based training session (delivered by a regional trial coordinator or member of the University research team) and detailed procedures manual, both of which provide an overview of the trial and detailed recruitment procedures (including judging how and when to approach patients, capacity for consent, scripts, and FAQs). Following the powerpoint training, the trainer will supervise each recruiter for approximately 2-4 hours as he or she commences patient recruitment in the practice waiting room. Ongoing support, advice, and troubleshooting will be provided by trial coordinators and University staff through regular meetings and practice visits.

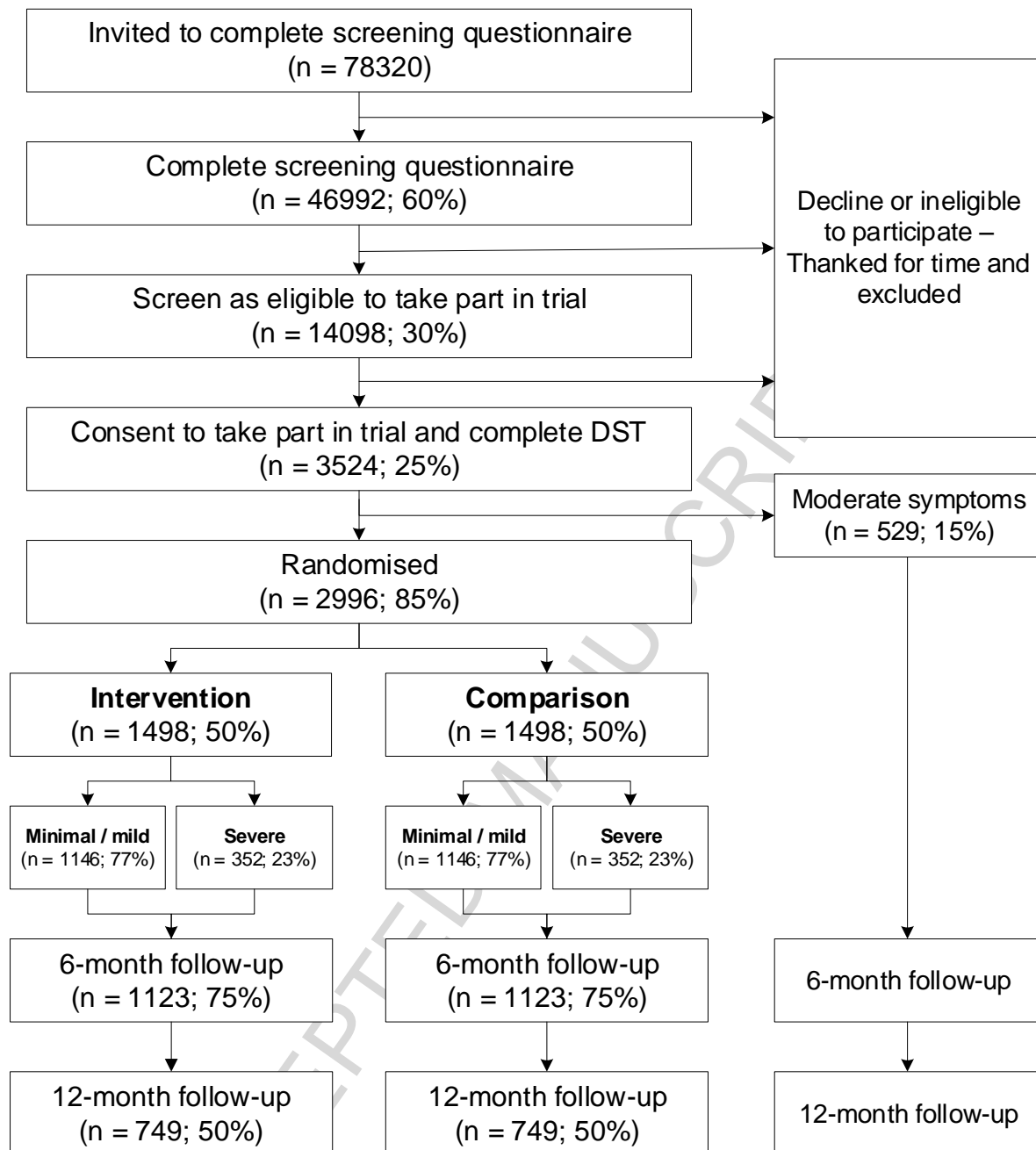


Figure 2. Expected participant progression through the trial

* Percentages for minimal/mild (76.5%) and severe (23.5%) groups are rounded to nearest whole number.

Strategies implemented to achieve the required sample size will include PHN staff working with participating practices to display posters and information pamphlets throughout each practice to raise awareness of the trial, and conducting engagement activities (e.g. lunchtime seminars) with GPs and practice staff to increase buy-in to the trial. The research team will also provide ongoing support and training for PHN staff (including care navigators, regional trial coordinators, and staff involved in patient recruitment), and will distribute a monthly trial newsletter to PHNs, who will be encouraged to distribute to practices in their catchment.

Data analysis

Descriptive statistics will be used to summarise socio-demographic and clinical characteristics of participants collected at baseline by trial arm and symptom severity. This will allow us to identify any imbalances between the two trial arms not addressed by randomisation.

Analysis will employ an intention-to-treat (ITT) approach [49], where all individuals randomised will be included in the analysis by their allocated trial arm status regardless of whether they received all, part or none of the intended treatments. For the primary analysis, we will use linear regression to estimate the difference in the mean K10 scores between the intervention and comparison arms at 6 months with adjustment for symptom severity group (minimal/mild vs. severe) and baseline K10 scores. Multiple imputation will be used to address attrition bias. Sensitivity analyses will be done using complete-cases only and with further adjustment for practice effects using random-intercept modelling of practice. Effect sizes will be presented on their original metric (with 95% confidence intervals and p-values) and as standardised mean differences.

We will also undertake sub-group analyses for the mild/minimal and severe symptom groups separately. For each sub-group, we will estimate differences in mean K10 scores at 6 months between the two arms, adjusting for baseline K10 scores and using multiple imputation. We will also undertake sensitivity analyses for the sub-group analyses using complete-case data and also adjusting for practice effects using a random intercept model. We will repeat all analyses (described for the primary outcome) using the 12-month K10 data and the secondary outcomes (depressive symptom severity, anxiety symptom severity and quality of life) measured at 6 and 12 months. We will also examine days out of role as a secondary outcome using negative binomial regression with effect sizes presented as rate ratios. In secondary analyses, we will adjust for pre-specified baseline participant characteristics (such as age, gender, education, Aboriginal and/or Torres Strait Islander status, use of medication for mental health). Sensitivity analyses using a pattern mixture model will be used to assess the robustness of the missing data assumption. We will also investigate the effects of non-compliance on the estimated treatment effects using a complier average casual effect (CACE) analysis [50]. A detailed statistical analysis plan will be made available prior to any statistical analysis of the primary and secondary outcomes. Analyses will be conducted in Stata 15.1 [51].

Economic evaluation

The framework for analysing the economic consequences of the clinical care coordination model will be a full economic evaluation using both a 'within trial' methodology as well as economic modelling to evaluate the population-level costs and impacts of a potential national roll-out from the perspective of the health care sector although a partial societal perspective will also be adopted. The health sector includes cost borne by the government as a third party payer as well as out of pocket costs incurred by patients for the direct costs of medical care. The partial societal perspective will also add on any productivity impacts observed in the trial (both absenteeism and presenteeism).

The economic evaluation will analyse data for the minimal/mild and severe symptom groups both separately and in tandem. It is hypothesised that the cost of providing more coordinated and tailored care for the severe symptom group will be offset by providing a more efficient model of care to participants within the minimal/mild symptoms. The within trial economic evaluation will consider the cost to deliver the low intensity and care navigation interventions (including the DST), the cost of suggested services to assist individuals as well as the cost of additional health care and

related resources utilised by participants during the trial and subsequent follow-up period. The DST costs will include development and maintenance costs. However, to avoid overestimating the per person costs (by assigning them only to trial participants) we will estimate the number of people who are likely to receive the intervention when implemented within the Australian population using assumptions based on the published literature.

For the minimal/mild symptom group, the number, type and cost of low-intensity services accessed will be collected through the resource use questionnaire. For the severe symptom group, the cost of care navigators' time will be based on an hourly wage rate plus overhead costs. The services recommended to the individual participants as part of care navigation will be collected within the trial database. These services will be costed based on the length and number of contacts with health professionals or when the services are outside of the health care system conservative estimates of cost will be sourced from reliable Australian sources.

For both symptom severity groups, the cost of individual participants' broader mental health related resource use will also be considered to evaluate any differences in overall costs and determine if substitution effects have occurred. Given that information on resource use will be obtained from several sources, we will ensure as much as possible that double counting of resources and costs does not occur.

In Australia the preferred outcome measure in health economic evaluations is the quality adjusted life year (QALY) because cost-effectiveness ratios using QALYs have inherent value-for-money connotations (current evidence suggests a threshold of around AU\$28,000/QALY) [52]. The Australian value set for the EQ-5D-5L will be used to derive utility values at each time point [53], although the more commonly used UK value set [54] will also be used in a sensitivity analysis. The utility values at each time point will then be used to calculate total QALYs for each participant using the area under the curve method [55]. Repeated measures ANOVA will be used to evaluate the change in utility values over the course of the trial between groups while generalised linear models will be used to compare the total QALYs between groups. Since the primary outcome is the K10 score, this will also be utilised as an additional outcome measure in the economic analysis, referred to as a cost-consequence analysis.

The economic evaluation will first measure and value any change to the use of health care resources over the observation period for those in the intervention and comparison arms, and then compare any additional costs to the additional outcomes achieved. Standard economic evaluation techniques including incremental analysis of mean differences and bootstrapping to determine confidence intervals will be used in the evaluation. If we find that there is an increased cost to providing the low intensity or care coordination services compared to usual practice we will also be able to estimate whether the incremental cost-effectiveness ratio falls below normally accepted value-for-money thresholds [56]. Extensive sensitivity analyses will also be undertaken to determine how robust the results are to some of the analytical assumptions (for example, variation in utility algorithm used and unit costs). A detailed economic analysis plan will be made available prior to analysis of the economic endpoints.

We will then use the costs and outcomes data to evaluate the population cost-effectiveness of the intervention using economic modelling techniques. The modelling will incorporate two main extra components, the first being the costs of rolling out the Link-me interventions at an Australian population level – including both approaches to the mild and severe symptom severity groups.

Secondly, the potential longer-term health benefits (and costs) at a population level will also be estimated. This will be undertaken using the epidemiological literature to estimate longer term trajectories of severity states as well as resource use implications. The precise structure of the economic model will partly depend on the final trial results, particularly any heterogeneity in outcomes observed, but is likely to be an expected value cohort analysis rather than a microsimulation. The merit of alternative model structures such as a discrete event simulation will also be considered [57].

Process evaluation

Qualitative and quantitative data will be collected throughout the trial to inform our understanding of what the enablers and challenges were for the implementation of the Link-me trial in general practices. Descriptions of the general practice context including relevant local community information, practice size, professional mix, co-located services and professionals, and patient flow will be developed from completed practice surveys and regular trial coordination meetings. This contextual data will be used in conjunction with data collected via semi-structured interviews with key stakeholders such as regional trial coordinators (n=3) and care navigators (1-2 per participating PHN). In addition, three focus groups are planned (one per participating PHN), in which up to ten GPs per group will be asked to share their views about care navigation processes and the experiences of having this model delivered within their practices. Where GPs may not be able to attend a focus group they will be provided with the opportunity to complete a telephone interview instead. The interview and focus group data will inform identification and evaluation of the barriers and enablers to implementation of the Link-me intervention to assess questions of sustainability and scalability. These interviews will be supplemented with further interview data collected with a sub-group of patients allocated to the intervention arm of the trial (10 per severity group per PHN for a total of 30 participants in the mild symptom group and 30 in the severe symptom group). Patient interviews will focus on their experiences of the intervention with attention to the ways it could be enhanced.

Normalisation Process Theory (NPT) will be employed as a theoretical framework for the process evaluation data analysis. Four main constructs underpin NPT: coherence, cognitive agreement, collective organisation and reflexive monitoring. Each of these constructs provides areas for examination in the implementation and evaluation of an intervention. The constructs are considered to be the 'mechanisms by which the work of implementation is operationalised' [58]. Coherence is concerned with how well an intervention is understood by the agents involved (this may be from a professional viewpoint or a patient viewpoint depending on the intervention and evaluation focus). Coherence asks *how well people understand the intervention and share in its benefits?* More than this, the construct of coherence refers to the processes and work undertaken by people to promote or inhibit routine embedding of a practice. Cognitive participation involves *how much people participate in the intervention—how committed and engaged are they in intervention?* Cognitive participation seeks to illuminate processes and work that individuals and organisations have to go through to enrol individuals to engage with the new practice. Collective action explores *the roles, activities and skill sets required for the intervention including how well the intervention fits within overall goals and activities of an organisation and compatibility with existing work practices*. The construct of collective action has four subcomponents related to contextual integration, relational integration, interactional workability and skill set workability. Reflexive monitoring involves the *engagement in activities to appraise and monitor the intervention and its outcomes*. Reflexive

monitoring is about informal and formal appraisal by individuals to assess advantages and disadvantages [59, 60].

To evaluate the implementation of Link-me using NPT principles, the four constructs and the underlying elements will be employed as a framework for analysis from trial establishment to completion. For example, to evaluate trial establishment, qualitative data collected via regular meetings, quarterly workshops and interviews conducted with key stakeholders will be analyzed for the ways in which the trial was understood, and the processes used to embed Link-me in PHNs and general practices. This will also include the assessment of the trial fit within organizational goals and activities, and the appraisal mechanisms available for assessment to explore advantages and disadvantages. The establishment data will be combined with analysis of the implementation of the interventions. For example, for participants allocated to the minimal/mild intervention group, telephone interview responses will be reviewed and analyzed for descriptions of receiving information for low intensity service options and how they engaged with this support. These descriptions will enable the research team to evaluate if there were shared understandings about the intervention, and the discussions about adoption (or non-adoption) of support will allow for exploration of cognitive participation. For care navigation, interviews and focus group transcripts will be reviewed for descriptions from different stakeholder groups about care navigation entailed. These descriptions will be compared with how they accord or otherwise with the research team's description of care navigation. In this analysis, it will be possible to determine where there were shared understandings or differences in interpretations of care navigation. It will also be possible to identify references that are made by different stakeholders to the processes that might have enhanced or restricted the embedding of care navigation as a practice within organisations. For cognitive participation in care navigation, data will be reviewed to identify processes and work that participants refer to as strategies for the enrolment of individuals in care navigation. This analytic process will continue with the additional constructs of collective action and reflexive monitoring applied also to the interview and focus group data.

Monitoring

Link-me will be monitored by the trial Steering Committee (SC) and an independent Evaluation Advisory Group (EAG). The SC will be comprised of all named investigators, the trial coordinator, a biostatistician, and a health economist. The SC will meet monthly to finalise trial materials and procedures, monitor progress, troubleshoot any areas of concern or safety requirements, ensure that the trial is being conducted according to protocol, and identify additional training or support required by the project team.

The EAG will comprise representatives of professional bodies (GPs, psychiatrists, psychologists, and mental health nurses), PHNs, and consumers and carers. It will act as a monitoring committee and meet biannually to monitor trial process and progress; advise on protocol modifications; and consider any adverse events and possible harms and the implications of these for the continuation of the trial. Given these terms of reference, a separate Data Monitoring Committee will not be established.

Adverse events

In light of the fact that the services recommended in the trial (both low intensity and those identified during care navigation) are also available to individuals outside the trial, and all participants are

linked in with health services, no interim analyses or auditing are planned to determine harm from the intervention directly.

All participants reporting high levels of suicidal ideation in baseline or follow-up surveys (indicated by a response of “nearly every day” to question 9 on the PHQ-9: “thoughts that you would be better off dead or of hurting yourself in some way”) will be contacted by a care navigator (at baseline) or trained research assistant (at follow up) for a structured risk assessment, regardless of trial arm or symptom severity group. This will be reported as an adverse event but is unlikely to result in treatment discontinuation or modification.

Up to three attempts will be made to contact participants for this risk assessment, and the GP will be alerted in writing (using a standardised template) if the participant is uncontactable or reports intent to hurt him/herself. Communication of the risk assessment outcome to the GP will be documented in the online data collection system. All participants triggering this risk assessment will be encouraged to make contact with their GP, and reminded of community-based resources such as Lifeline (and re-sent the contact list provided on enrolment in the trial if necessary).

Passive surveillance of harms will also be in place throughout the trial and may be reported by participants or GPs (e.g. in an interview as part of the process evaluation, or by contacting the Link-me team via the contact details on the plain language statement). Adverse events may also be disclosed in the context of care navigation, in which case the care navigator will record the event within the online administration portal and inform the trial manager. The trial manager will record severity, potential for the event to have been anticipated, and action taken, and report this to the SC and EAG. Serious adverse events will also be reported to the University of Melbourne Human Research Ethics Committee (HREC) and evaluated by the trial lead who is a trained clinician.

Ethics and dissemination

This protocol has been approved by the University of Melbourne HREC (ID: 1749832). Collection of routine government data within the MBS and PBS has been approved by the Commonwealth Department of Human Services (ID: M18420). Collection of headspace data has been approved by headspace National Office, and collection of PMHC MDS data has been approved by the Commonwealth Department of Health. Approval from these bodies applies to all trial sites. Any substantive modifications to this protocol that affect the conduct or nature of the trial will be submitted to the responsible HREC for approval prior to implementation.

Regardless of the magnitude or direction of effect, the results of this trial will be submitted to the Department of Health, with the final report due in September 2020. The trial will be reported following the CONSORT guidelines [61] and the process evaluation results detailed for further interpretation and analysis of effects. Subject to approval by the Department, the trial outcomes and evaluation may also be presented at relevant research conferences and as published articles in peer-reviewed journals. Authorship eligibility guidelines at the respective institutions and for journals will be followed.

The results of the trial will be communicated to participants via a trial newsletter and to the involved general practices via personal visits and community reports. The de-identified dataset and statistical code may be provided on request, with permission from the Department of Health.

Trial status

Link-me was prospectively registered on the Australian and New Zealand Clinical Trials Registry (ACTRN 12617001333303) in September 2017. Participant recruitment commenced in November 2017 and is anticipated to be completed in October 2018, with data collection ceasing 12 months later.

Discussion

Stepped mental health care is both recommended by clinical guidelines [24, 62, 63] and a focus of current policy direction in Australia [12]. However, tools to guide decisions around which ‘step’ of care to allocate an individual to are lacking. This is a particular problem for general practice, where the vast majority of mental health problems are identified and managed [64]. Our *diamond* study found that almost one quarter of patients met criteria for probable depression [47], and mental health concerns account for just over 12 percent of all GP encounters [65]. The sometimes significant work associated with assessment, treatment, and referral of these problems may impose a disproportionate burden on GPs’ time.

Decision support tools completed prior to a consultation may assist GPs with the task of identifying the mental health needs of patients and assist patients to identify goals. By encouraging patients with minimal or mild symptoms to access low intensity services, it may be possible to reserve more intensive treatments for patients with greater needs. In Link-me, patients predicted to have severe symptoms are offered an intervention referred to as care navigation – support from a trained and registered professional to navigate the health care system and access appropriate services. Unique to this intervention, patients can access additional funding (via a care package) to support services outside the mental health system, where those services are considered essential to improving mental health. This novel approach aims to address the multimorbidity (mental, physical, and social) common to this group that presents a number of challenges to care and often results in poor clinical outcomes [66, 67].

Link-me will evaluate both the clinical effectiveness and economic value of implementing this model of care. We will assess the extent to which savings accrued from streaming people with mild symptoms to less intensive service options might offset any additional costs of care navigation and individually tailored care packages for people with severe symptoms. As a large-scale stratified individually randomised trial of a complex intervention, Link-me represents a unique opportunity to contribute to evidence-based mental health policy and guide the development and implementation of stepped care models in Australia. The trial is being undertaken with scalability in mind and analyses will consider the economic and service delivery implications of a national roll-out of the model of care it is testing. The results are planned to be reported directly to the Australian Government and will inform how mental health services across Australia are funded and delivered in the future.

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these studies and for making the current trial possible. Thanks also to the PHN Lead Sites and Department of Health for their contribution to the development and implementation of the Link-me trial.

Role of the funding source

Link-me is funded by the Australian Commonwealth Department of Health, who also assisted to refine the study design and provided approval of both protocol itself and the submission of this manuscript for publication. The funders will have no role in the collection or analysis of data.

Declaration of competing interests

The authors declare that they have no competing interests with respect to the research, authorship, and/or publication of this paper.

References

1. Whiteford HA, Ferrari AJ, Degenhardt L, Feigin V, Vos T. The global burden of mental, neurological and substance use disorders: An analysis from the Global Burden of Disease Study 2010. *PLoS One*. 2015 Feb 6;10(2). PMID: WOS:000349444900070.
2. Barbour V, Clark J, Connell L, Ross A, Simpson P, Winker M, et al. The paradox of mental health: Over-treatment and under-recognition. *PLoS Medicine*. 2013 May;10(5). PMID: WOS:000319670900030. doi: 10.1371/journal.pmed.1001456.
3. Crome E, Baillie AJ. Better Access and equitable access to clinical psychology services: What do we need to know? *Medical Journal of Australia*. 2016 May 16;204(9):341-3. PMID: WOS:000410552500010. doi: 10.5694/mja15.01393.
4. Harris M, Hobbs M, Burgess P, Pirkis J, Diminic S, Siskind D, et al. Frequency and quality of mental health treatment for affective and anxiety disorders among Australian adults. *Medical Journal of Australia*. 2015;202(4):185-9.
5. Bower P, Gilbody S, Richards D, Fletcher J, Sutton A. Collaborative care for depression in primary care. Making sense of a complex intervention: Systematic review and meta-regression. *British Journal of Psychiatry*. 2006 2006;189:484-93. PMID: MEDLINE:17139031.
6. van Straten A, Hill J, Richards DA, Cuijpers P. Stepped care treatment delivery for depression: A systematic review and meta-analysis. *Psychological Medicine*. 2015;45(02):231-46.
7. Smith SM, Wallace E, O'Dowd T, Fortin M. Interventions for improving outcomes in patients with multimorbidity in primary care and community settings. *Cochrane Database of Systematic Reviews*. 2016 (3). PMID: WOS:000373475200014.
8. Salisbury C, Man MS, Bower P, Guthrie B, Chaplin K, Gaunt DM, et al. Management of multimorbidity using a patient-centred care model: A pragmatic cluster-randomised trial of the 3D approach. *Lancet*. 2018 Jul 7;392(10141):41-50. PMID: WOS:000437665000032.
9. Bassilios B, Nicholas A, Reifels L, King K, Fletcher J, Machlin A, et al. Achievements of the Australian Access to Allied Psychological Services (ATAPS) program: Summarising (almost) a decade of key evaluation data. *International Journal of Mental Health Systems*. 2016;10:61. PMID: 27708698. doi: 10.1186/s13033-016-0092-4.
10. Australian Institute of Health and Welfare. Mental health services in Australia: Medicare services. 2018 [cited 2018 July]; Available from: <http://www.aihw.gov.au/reports/mental-health-services/mental-health-services-in-australia/report-contents/medicare-services>.
11. National Mental Health Commission. The National Review of Mental Health Programmes and Services. Sydney: National Mental Health Commission, 2014.
12. Australian Government. Australian Government Response to Contributing Lives, Thriving Communities – Review of Mental Health Programmes and Services. Canberra: Australian Government, 2015.
13. Department of Health. Primary Health Networks: Grant Programme Guidelines: Annexure 1 - Primary Mental Health Care. Canberra: Australian Government; 2016.
14. Wachtler C, Coe A, Davidson S, Fletcher S, Mendoza A, Sterling L, et al. Development of a mobile clinical prediction tool to estimate future depression severity and guide treatment in primary care: User-centred design. *JMIR Mhealth and Uhealth*. 2018;6(4):e95. doi: 10.2196/mhealth.9502.
15. Gunn J, Wachtler C, Fletcher S, Davidson S, Mihalopoulos C, Palmer V, et al. Target-D: A stratified individually randomized controlled trial of the diamond clinical prediction tool to triage and target treatment for depressive symptoms in general practice: Study protocol for a randomized controlled trial. *Trials*. 2017;18:342. doi: 10.1186/s13063-017-2089-y.
16. Chondros P, Davidson S, Wolfe R, Gilchrist G, Dowrick C, Griffiths F, et al. Development and validation of a prognostic model for predicting depression severity in adult primary patients with depressive symptoms using the diamond longitudinal study. *Journal of Affective Disorders*. 2018;227:854-60. doi: 10.1016/j.jad.2017.11.042.
17. Australian Bureau of Statistics. National Survey of Mental Health and Wellbeing: Summary of results. Canberra: ABS; 2008.

18. Chan A, Tetzlaff J, Altman D, Laupacis A, Gøtzsche P, Krleža-Jerić K. SPIRIT 2013 statement: Defining standard protocol items for clinical trials. *Annals of Internal Medicine*. 2013;158. doi: 10.7326/0003-4819-158-3-201302050-00583.
19. Kroenke K, Spitzer RL, Williams JBW. The Patient Health Questionnaire-2: Validity of a two-item depression screener. *Medical Care*. 2003 Nov;41(11):1284-92. PMID: WOS:000186270500008. doi: 10.1097/01.Mlr.0000093487.78664.3c.
20. Kroenke K, Spitzer RL, Williams JBW, Monahan PO, Lowe B. Anxiety disorders in primary care: Prevalence, impairment, comorbidity, and detection. *Annals of Internal Medicine*. 2007 Mar 6;146(5):317-25. PMID: WOS:000244829600001.
21. Dowrick C. Does testing for depression influence diagnosis or management by general practitioners? *Family Practice*. 1995 Dec;12(4):461-5. PMID: WOS:A1995TT31200016. doi: DOI 10.1093/fampra/12.4.461.
22. Valderas JM, Kotzeva A, Espallargues M, Guyatt G, Ferrans CE, Halyard MY, et al. The impact of measuring patient-reported outcomes in clinical practice: A systematic review of the literature. *Quality of Life Research*. 2008 Mar;17(2):179-93. PMID: WOS:000253130000001.
23. Titov N, Dear BF, Staples LG, Bennett-Levy J, Klein B, Rapee RM, et al. MindSpot clinic: An accessible, efficient, and effective online treatment service for anxiety and depression. *Psychiatric Services*. 2015 Oct;66(10):1043-50. PMID: WOS:000370727100012.
24. Malhi GS, Outhred T, Hamilton A, Boyce PM, Bryant R, Fitzgerald PB, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders: major depression summary. *Medical Journal of Australia*. 2018 Mar 5;208(4):175-80. PMID: WOS:000429509000014.
25. Cromarty P, Drummond A, Francis T, Watson J, Battersby M. NewAccess for depression and anxiety: adapting the UK Improving Access to Psychological Therapies Program across Australia. *Australasian Psychiatry*. 2016 Oct;24(5):489-92. PMID: WOS:000384836800021.
26. Flett JAM, Hayne H, Riordan B, Thompson L, Conner T. Mobile mindfulness meditation: A randomised controlled trial of the effect of two popular apps on mental health. *Mindfulness*. 2018.
27. Department of Health. Fact sheet: Primary Health Networks. 2018 [cited 2018 August]; Available from: <http://www.health.gov.au/internet/main/publishing.nsf/Content/Fact-Sheet-Primary-Health-Networks>.
28. Dalton H, Read D, Handley T, Perkins D. Low intensity mental health services: A rapid review - January 2017. Orange: Centre for Rural and Remote Mental Health, University of Newcastle; 2017.
29. Gunn J, Diggins J, Hegarty K, Blashki G. A systematic review of complex system interventions designed to increase recovery from depression in primary care. *BMC Health Services Research*. 2006;6(1):88. PMID: doi:10.1186/1472-6963-6-88.
30. Archer J, Bower P, Gilbody S, Lovell K, Richards D, Gask L, et al. Collaborative care for depression and anxiety problems. *Cochrane Database of Systematic Reviews*. 2012. PMID: 11687187. doi: 10.1002/14651858.CD006525.pub2.
31. Thota AB, Sipe TA, Byard GJ, Zometa CS, Hahn RA, McKnight-Eily LR, et al. Collaborative care to improve the management of depressive disorders: A community guide systematic review and meta-analysis. *American Journal of Preventive Medicine*. 2012 May;42(5):525-38. PMID: WOS:000302963300020. doi: 10.1016/j.amepre.2012.01.019.
32. Miller CJ, Grogan-Kaylor A, Perron BE, Kilbourne AM, Woltmann E, Bauer MS. Collaborative chronic care models for mental health conditions: Cumulative meta-analysis and metaregression to guide future research and implementation. *Medical Care*. 2013 Oct;51(10):922-30. PMID: WOS:000324751000011.
33. Gunn JM, Ayton DR, Densley K, Pallant JF, Chondros P, Herrman HE, et al. The association between chronic illness, multimorbidity and depressive symptoms in an Australian primary care cohort. *Social Psychiatry and Psychiatric Epidemiology*. 2012;47(2):175-84.
34. McKenzie KJ, Pierce D, Gunn JM. Guiding patients through complexity. *Australian journal of general practice*. 2018;47(1-2):8-13.

35. Soares J, Jeff Wu CF. Some restricted randomization rules in sequential designs. *Communications in Statistics - Theory and Methods*. 1983;12:2017-34. doi: 10.1080/03610928308828586.
36. Kessler RC, Andrews G, Colpe LJ, Hiripi E, Mroczek DK, Normand SLT, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychological Medicine*. 2002 Aug;32(6):959-76. PMID: WOS:000177600500002. doi: 10.1017/S0033291702006074.
37. Australian Bureau of Statistics. Use of the Kessler Psychological Distress Scale in ABS Health Surveys, Australia, 2007-08. 2012 [cited 2018 August]; Available from: <http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/4817.0.55.001Chapter92007-08>.
38. Department of Health. Primary mental health care minimum data set: Overview of purpose, design, scope and key decision issues. Canberra: Australian Government; 2016.
39. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine*. 2001 Sep;16(9):606-13. PMID: WOS:000171184700005. doi: 10.1046/j.1525-1497.2001.016009606.x.
40. Arroll B, Goodyear-Smith F, Crengle S, Gunn J, Kerse N, Fishman T, et al. Validation of PHQ-2 and PHQ-9 to screen for major depression in the primary care population. *Annals of Family Medicine*. 2010 July 1, 2010;8(4):348-53. doi: 10.1370/afm.1139.
41. McMillan D, Gilbody S, Richards D. Defining successful treatment outcome in depression using the PHQ-9: A comparison of methods. *Journal of Affective Disorders*. 2010;127(1-3):122-9. doi: 10.1016/j.jad.2010.04.030.
42. Spitzer RL, Kroenke K, Williams JBW, Lowe B. A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine*. 2006 May 22;166(10):1092-7. PMID: WOS:000237720500008. doi: 10.1001/archinte.166.10.1092.
43. Herdman M, Gudex C, Lloyd A, Janssen MF, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of Life Research*. 2011 Dec;20(10):1727-36. PMID: WOS:000297348200023. doi: 10.1007/s11136-011-9903-x.
44. Janssen MF, Pickard AS, Golicki D, Gudex C, Niewada M, Scalone L, et al. Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: A multi-country study. *Quality of Life Research*. 2013;22(7):1717-27.
45. Chatterton ML, Chambers S, Occhipinti S, Girgis A, Dunn J, Carter R, et al. Economic evaluation of a psychological intervention for high distress cancer patients and carers: Costs and quality-adjusted life years. *Psycho-Oncology*. 2016 Jul;25(7):857-64. PMID: WOS:000380015900014. doi: 10.1002/pon.4020.
46. Chatterton ML, Mihalopoulos C, O'Neil A, Itsiopoulos C, Opie R, Castle D, et al. Economic evaluation of a dietary intervention for adults with major depression (the "SMILES" trial). *Bmc Public Health*. 2018 May 22;18. PMID: WOS:000432722400001.
47. Gunn J, Gilchrist G, Chondros P, Ramp M, Hegarty K, Blashki G, et al. Who is identified when screening for depression is undertaken in general practice? Baseline findings from the Diagnosis, Management and Outcomes of Depression in Primary Care (diamond) longitudinal study. *Medical Journal of Australia*. 2008;188(12 Suppl):S119-25.
48. Richards DA, Bower P, Chew-Graham C, Gask L, Lovell K, Cape J, et al. Clinical effectiveness and cost-effectiveness of collaborative care for depression in UK primary care (CADET): A cluster randomised controlled trial. *Health Technology Assessment*. 2016 Feb;20(14):1-192. PMID: WOS:000371395600001. doi: 10.3310/hta20140.
49. White IR, Carpenter J, Horton NJ. Including all individuals is not enough: Lessons for intention-to-treat analysis. *Clinical Trials*. 2012 Aug;9(4):396-407. PMID: WOS:000307982600003. doi: 10.1177/1740774512450098.
50. Dunn G, Maracy M, Tomenson B. Estimating treatment effects from randomized clinical trials with noncompliance and loss to follow-up: The role of instrumental variable methods. *Stat Methods Med Res*. 2005;14. doi: 10.1191/0962280205sm403oa.

51. StataCorp. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC; 2017.
52. Edney LC, Haji Ali Afzali H, Cheng TC, Karnon J. Estimating the reference incremental cost-effectiveness ratio for the Australian health system. *Pharmacoeconomics*. 2018 Feb;36(2):239-52. PMID: 29273843. doi: 10.1007/s40273-017-0585-2.
53. Viney R, Norman R, Brazier J, Cronin P, King MT, Ratcliffe J, et al. An Australian discrete choice experiment to value EQ-5D health states. *Health Economics*. 2014 Jun;23(6):729-42. PMID: 23765787. doi: 10.1002/hec.2953.
54. EuroQol. EQ-5D 5L valuation. 2018 [cited 2018 August]; Available from: <https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/valuation/>.
55. Glick HA, Doshi JA, Sonnad SS, Polsky D. *Economic evaluation in clinical trials*. Oxford: Oxford University Press; 2014. ISBN: 0191508055.
56. Mihalopoulos C, Vos T, Pirkis J, Carter R. The economic analysis of prevention in mental health programs. *Annual Review in Clinical Psychology*. 2011;7:169-201.
57. Briggs AH, Claxton K, Sculpher M. *Decision modelling for economic evaluation*. Oxford: Oxford University Press; 2006.
58. May CR, Rapley T, Mair FS, Treweek S, Murray E, Ballini L, et al. Normalization Process Theory online users' manual, toolkit and NoMAD instrument. 2015 [cited 2018 August]; Available from: <http://www.normalizationprocess.org/>.
59. Gunn JM, Palmer VJ, Dowrick CF, Herrman HE, Griffiths FE, Kokanovic R, et al. Embedding effective depression care: Using theory for primary care organisational and systems change. *Implementation Science*. 2010 Aug 6;5. PMID: WOS:000282308800001.
60. May CR, Finch T, Ballini L, MacFarlane A, Mair F, Murray E, et al. Evaluating complex interventions and health technologies using normalization process theory: Development of a simplified approach and web-enabled toolkit. *BMC Health Services Research*. 2011 Sep 30;11. PMID: WOS:000296338200002.
61. Schulz KF, Altman DG, Moher D, Grp C. CONSORT 2010 Statement: Updated guidelines for reporting parallel group randomised trials. *BMC Medicine*. 2010 Mar 24;8. PMID: WOS:000277073000001.
62. National Institute for Health and Care Excellence. *Depression: The treatment and management of depression in adults (updated edition)*. London: NICE; 2010.
63. Andrews G, Bell C, Boyce P, Gale C, Lampe L, Marwat O, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of panic disorder, social anxiety disorder and generalised anxiety disorder. *Australian and New Zealand Journal of Psychiatry*. 2018;52(12):1109-72.
64. Burgess PM, Pirkis JE, Slade TN, Johnston AK, Meadows GN, Gunn JM. Service use for mental health problems: Findings from the 2007 National Survey of Mental Health and Wellbeing. *Australian and New Zealand Journal of Psychiatry*. 2009;43(7):615-23. PMID: WOS:000267012100005.
65. Britt H, Miller GC, Henderson J, Bayram C, Harrison C, Valenti L, et al. *General practice activity in Australia 2015-16*. Sydney: Sydney University Press; 2016.
66. Knowles SE, Chew-Graham C, Adeyemi I, Coupe N, Coventry PA. Managing depression in people with multimorbidity: A qualitative evaluation of an integrated collaborative care model. *Bmc Family Practice*. 2015 Mar 5;16. PMID: WOS:000350856600001.
67. Wallace E, Salisbury C, Guthrie B, Lewis C, Fahey T, Smith S. Managing patients with multimorbidity in primary care. *British Medical Journal*. 2015;350:h176. doi: 10.1136/bmj.h176.